ISRCTN12678718 https://doi.org/10.1186/ISRCTN12678718

IIH Pressure - a new treatment for raised brain pressure in Idiopathic Intracranial Hypertension

Submission date
19/06/2017

Recruitment status
No longer recruiting

Registration date
18/07/2017

Overall study status
Completed

Last Edited
05/08/2024

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Idiopathic intracranial hypertension (IIH) is a condition of unknown cause. The condition is causes raised pressure in the brain and can cause daily headaches and loss of sight, which can be permanent. The raised brain pressure squashes the nerves supplying the eye (also known as papilloedema) and this can affect vision and cause blindness. Over 90% of patients with IIH are overweight and weight loss is the most effective treatment. Other treatments for IIH have very little current evidence to support their use and few treatments in general are available for raised brain pressure. Gut neuro-peptides are a group of hormones released by the gut with specific actions in the central nervous system. GLP-1 is a hormone that has known actions in the kidney to reduce blood pressure. Preliminary work has shown this mechanism to be similar to that regulating fluid secretion in the brain. Further preliminary work has shown that GLP-1 reduces intra-cranial pressure in animal models. GLP-1 drugs are currently used to treat diabetes and aid weight loss. The aim of this study is to investigate the effects of the GLP-1 drug, exenatide, on intra-cranial pressure as well as evaluate the effect of five common medications on intra-cranial pressure.

Who can participate?
Females aged 18 to 60 years old who are diagnosed with IIH.

What does the study involve?
This study has two parts. The first part of the study includes participants having telemetric intra-cranial pressure sensors fitted. Participants are randomised to one of two groups. Those in the first group receive exenatide through skin injections twice daily for 12 weeks. Those in the second group receive a placebo (a dummy medication). This is given through skin injections twice daily for 12 weeks. Participants are followed up at two and 12 weeks with intracranial pressure recording (ICP) which is a non-invasive monitor, as well as blood tests, headaches scores and cognitive (mental) testing). At 12 weeks, participants are assessed for their quality of life, and clinical measurements. The second part of the study randomly allocates participants to receiving one of five medications for two weeks (with one week washout between them).

What are the possible benefits and risks of participating?
Participants may benefit from receiving brain pressure monitors which is non-invasive and can

improve monitoring. Participants may benefit from improvements in their conditions depending on the medication they receive. Participants may benefit from increased clinical observation during the study period as well as opportunities to improve their understanding of their condition. There is a small risk from using anesthesia as well as small risks from the procedure of bleeding near the brain, infection or seizures after the procedure. There is a small risk that the device could fail which requires another surgery to remove the device.There is a risk of nausea due to the medication. There are rare reports of pancreatitis associated with the medication.

Where is the study run from?
This study is being run by the University of Birmingham (UK) and takes place in six health centres /hospitals in the UK.

When is the study starting and how long is it expected to run for?
June 2015 to July 2019

Who is funding the study?
Ministry of Defence (UK)

Who is the main contact?
Mr James Mitchell

Contact information

Type(s)
Public

Contact name
Mr James Mitchell

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

CPMS 34681

Study information

Scientific Title
The acute and chronic effects of gut neuropeptides on intracranial pressure regulation

Acronym
IIH Pressure

Study objectives
Exenatide modulates fluid secretion and inflammatory biomarkers in the central nervous system following acute administration.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Midlands Research Ethics Committee - Solihull, 29/06/2017, ref: 17/WM/0179

Study design
Randomized; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Idiopathic intracranial hypertension

Interventions
The main part of the trial has two arms, active treatment and placebo. The second part of the trial is single arm and open to all participants on the main trial.

First part of the study:
The randomisation process for the main trial is by computer generated list.

The active treatment arm receives a single bolus of the study drug, exenatide at baseline. The dose is 20 mcg Exenatide (Byetta) via subcutaneous injection. Following the baseline day all active arm participants receive 10 mcg Exenatide (Byetta) via subcutaneous injection twice daily and self administer. The duration of treatment is 12 weeks. Follow-up takes place at 2 weeks and 12 weeks.

The placebo arm receives a single bolus of Normal Saline Placebo at baseline. The dose includes 1 mL via subcutaneous injection. Following the baseline day all placebo arm participants receive 0.5 mL Normal Saline via subcutaneous injection twice daily and will self administer. The duration of treatment will be 12 weeks. Follow-up is done at two weeks and 12 weeks.

Follow up is done at two and 12 weeks where participants undergo Intracranial pressure (ICP) recording, IOP, blood sampling, OCT, headache scores and cognitive testing. Additionally, at 12 weeks participants also undergo clinical measurements, quality of life questionnaires, and DEXA scan.

Second part of the study:
This part of the study is a single arm sequential, open label design. All participants receive all medications in random order. The duration of treatment is two weeks, week one is a titration week where necessary. There will be a minimum one week washout between rounds. Follow-up is by visit at two weeks.

The medications for this part of the study are:

Acetazolomide: Patients take 500 mg BD PO immediate release for 7 days, followed by 1g BD for 7 days.
Spironolactone: Participants take 100 mg OD PO for 7 days, followed by 200 mg OD for 7 days.
Amiloride: Participants take 10 mg OD PO for 14 days.
Furosemide: Patients take 40 mg OD PO for 7 days, followed by 80 mg OD for 7 days.
Topiramate: Participants take 25mg BD PO for 4 days, followed by 25 mg mane/50 mg nocte for 3 days followed by 50 mg BD for 7 days.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Exenatide, acetazolomide, spironolactone, amiloride, furosemide, topiramate

Primary outcome measure
1. Change in Intracranial pressure (ICP) measured by telemetric ICP catheter between baseline and 24 hours post drug administration
2. Change in ICP measured by telemetric ICP catheter between baseline and end of trial visit
3. Change in ICP measured by telemetric ICP catheter between baseline and 2.5 hours post administration

Secondary outcome measures
1. Biological effects of exenatide measured using blood tests at 24 h, 2 and 12 weeks
2. Headaches measured using severity scores at 24 h, 2 and 12 weeks

3. Quality of life measured using SF-36 at baseline and 12 weeks
4. CSF exenatide levels measured by assay at two and a half, six and 11 hours

Overall study start date
01/06/2015

Completion date
31/07/2019

Eligibility

Key inclusion criteria
1. Female
2. Aged 18-60 years old
3. Diagnosed with IIH by the modified Dandy criteria
4. Active disease (papilloedema Frisen grade greater than 1)
5. Significantly raised ICP (greater than 25cm CSF)
6. No evidence of venous sinus thrombosis (documented normal MR Venogram of CT Venogram)
6. Able to provide informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
Female

Target number of participants
Planned Sample Size: 16; UK Sample Size: 16

Total final enrolment
15

Key exclusion criteria
1. Aged less than 18 or older than 60 years
2. Pregnant or trying to conceive
3. Significant co-morbidity, such that in the opinion of the investigator it would not be in the participant’s best interest to participate in the trial
4. Addison’s or Cushing’s disease
5. Functioning CSF shunt/stent or optic nerve sheath fenestration
6. Currently using GLP-1 agonist or DPP-4 inhibitor
7. Surgical contra-indication

8. Concomitant therapy with acetazolomide, topiramate or diuretics (this can be discontinued 1 month prior to enrolment)
9. Inability to give informed consent e.g. due to cognitive impairment

Date of first enrolment
31/07/2017

Date of final enrolment
31/07/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2WG

Study participating centre
Sandwell General Hospital
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Study participating centre
Leicester General Hospital
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S10 2JF

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University Hospital Coventry and Warwickshire
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Sponsor information

Organisation
University of Birmingham

Sponsor details
Birmingham
Birmingham
England
United Kingdom
B15 2TT

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Ministry of Defence

Alternative Name(s)
MOD

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high impact, peer-reviewed journal, intent to publish by July 2019.

Intention to publish date
31/07/2019

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	Evaluation of telemetric intracranial pressure monitoring	01/11/2022	03/11/2022	Yes	No
Preprint results	Exenatide results	06/09/2022	07/11/2022	No	No
HRA research summary			28/06/2023	No	No
Abstract results		07/12/2022	05/08/2024	No	No
Other publications		01/12/2020	05/08/2024	Yes	No
Other publications	Sub-study	22/11/2023	05/08/2024	Yes	No